Acalculous Cholecystitis Due to Hodgkin's Disease

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ACUTE CHOLECYSTITIS is associated with stones in the gallbladder in more than 90 percent of the cases. When stones are present, the usual cause is impaction of one of them in the cystic duct.

In the patients in whom acute cholecystitis occurs without stones in the gallbladder, the precipitating cause is usually less obvious. Obstruction of the cystic duct may be due to neighboring inflammatory reaction, fibrosis, tumor, anomalous vessels, or kinks of the cystic duct.

A case of acute acalculous cholecystitis in a 70-year-old physician with carcinoma of the cystic duct has been reported.[1] There have been reports also of obstruction of the common bile duct secondary to Hodgkin's tumor masses.[2] In a review of the literature no report could be found of acalculous cholecystitis due to Hodgkin's involvement of the cystic duct, as occurred in the following case.

Report of a Case

The patient was a 44-year-old white man who was seen at the San Bernardino County General Hospital in early January of 1966 because of enlargement of a left cervical lymph node. Hodgkin's disease had been diagnosed in 1949 by a left supraclavicular lymph node biopsy. Local irradiation had brought about remission, the patient requiring no further treatment. In 1964 he had had myocardial infarction, and from then on had been troubled with angina pectoris. He was treated with anticoagulants and coronary vasodilators. Further examination at that time was unremarkable. Roentgenograms of the chest revealed a widened mediastinum. Biopsy of a left cervical node revealed recurrent Hodgkin's disease. On bronchoscopy, no abnormalities were noted. The patient was discharged and shortly after returning home he began having pain in the right upper quadrant of the abdomen, associated with anorexia and nausea. The pain was steady, intense and knife-like. It was not relieved by taking Maalox®* or Donnatal®†

On physical examination, the patient was noted to be in moderate distress. Oral temperature was 99.8° F. The pulse rate was 78 per minute. There was no jaundice. Local tenderness was present in the epigastrium and the right upper quadrant of the abdomen. All oral intake was stopped and fluids, antispasmodics and meperidine were administered intravenously.

Hemoglobin was 14 grams per 100 ml and the hematocrit was 42 percent. Leukocytes numbered 3,700 per cu mm and platelets 400,000 per cu mm. The proportion of reticulocytes was 0.8 percent. A review of previous hemograms revealed them to be essentially the same. Results of the VDRL test were negative. Urinalysis was within normal limits. An electrocardiogram was consistent with an old inferior myocardial infarction with some lateral ischemia. Roentgenograms of the chest revealed enlarged hilar lymph nodes. An upper gastrointestinal series was interpreted as normal. Attempts at oral cholecystography revealed nonvisualization of the gallbladder on two occasions, one with a double dose of dye. Liver functions and serum amylase were normal. No liver scan was obtained. The leukocyte count, determined several times, remained essentially unchanged.

Symptoms persisted and exploratory operation was done 10 January 1966. The gallbladder was noted to be thickened, erythematous and tense. An enlarged sentinel lymph node was present in Calot's triangle and a thickened, leathery, firm cystic duct was found (Figures 1 and 2). The gallbladder was removed by sharp dissection. No gallstones were present. The liver, spleen, periaortic lymph nodes and iliac lymph nodes were

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*Magnesium-aluminum hydroxide.

†A compound of hyoscamine sulfate, atropine sulfate, hyoscine hydrobromide and phenobarbital (Robins).

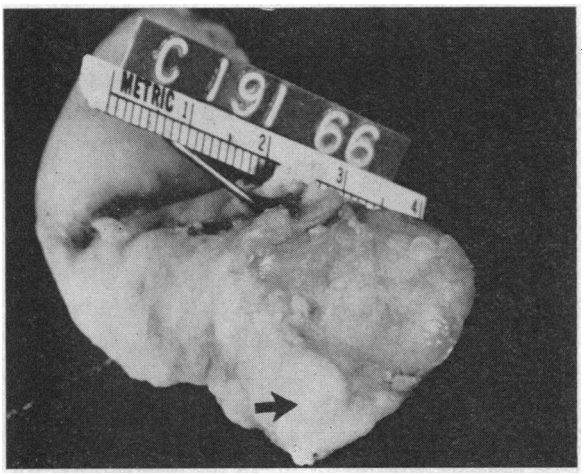

Figure 1. — Thickened cystic duct with small lumen is seen (arrow). The enlarged lymph node is seen adjacent to the cystic duct.

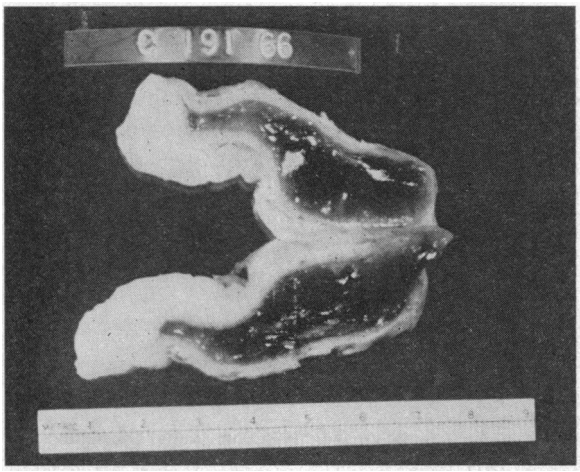

Figure 2.—Sagittal section of the cystic duct and gallbladder shows the thickened area of the cystic duct occluding the lumen.

found to be involved with what appeared to be Hodgkin's disease.

The postoperative course was uneventful and on 3 February the patient was given an intravenous injection of nitrogen mustard, 0.4 mg per kg of body weight. This was followed by oral administration of cyclophosphamide.

Histologic examination revealed Hodgkin's disease of the gallbladder in the area of the cystic duct. Foci of infiltrations of chronic inflammatory cells were seen in the fundus of the gallbladder. Multinucleated Dorothy Reed-Sternberg cells were frequent (Figure 3).

The patient is observed regularly in the outpatient department. Hydralazine (Apresoline®) and reserpine are given for hypertension. He has had several courses of intravenous nitrogen mustard and is currently receiving cyclophosphamide by mouth. When last seen, in September of 1969, he was doing well.

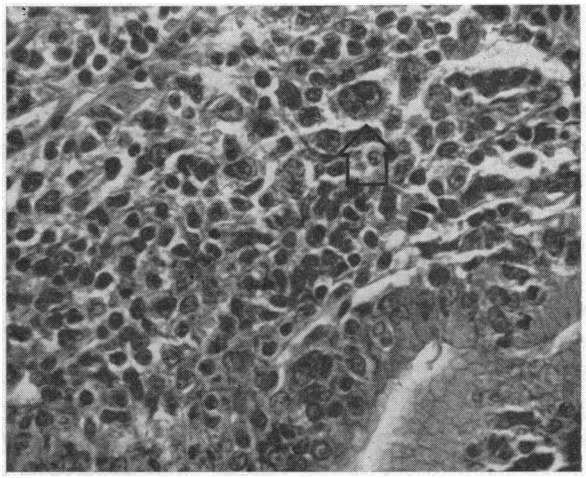

Figure 3.—The cystic duct epithelium is evident at the lower right in the illustration. Dorothy Reed-Sternberg cells are present (arrow) as well as granulocytes, fibroblasts, lymphocytes, monocytes and plasma cells. Minimal fibrosis is present. (Hematoxylin & Eosin, × 570.)

Discussion

Progressive cholecystitis usually is manifested by rising fever and pulse rate, increasing right upper quadrant abdominal pain and increasing leukocytosis. It usually follows impaction of a gallstone in the cystic duct. As the gallbladder distends, it becomes more inflamed and perforation may occur.

The clinical symptoms in the present case differed in that the usual signs of acute inflammation were absent, there was no significant rise in temperature or pulse rate, and leukocyte count remained essentially unchanged. However, the right upper quadrant abdominal pain remained localized and did not improve.

Primary or secondary lesions of Hodgkin's disease may arise anywhere along the gastrointestinal tract. However, the lesions most often occur in the stomach and small bowel. There has been no previous recorded case of Hodgkin's disease of the cystic duct causing cholecystitis. Most of the lesions of the alimentary tract are associated with a generalized disease. In the more advanced cases of Hodgkin's disease, some involvement of the liver is quite common. This may be evaluated by liver scanning techniques. Jaundice and ascites

may accompany the hepatic enlargement. Whether jaundice is to be explained by the assumption of deposit of the disease at the portal area or intrahepatic biliary tract obstruction, or hepatocellular disease of viral causation, may be an intriguing diagnostic problem. The results of liver function tests may be equivocal. In a study by Levitan, Diamond and Craver[3] the liver was noted to be the seat of some lesion in two-thirds of 112 cases of Hodgkin's disease that came to postmortem examination. Diffuse infiltration was the most common type of lesion. The symptoms of obstructive jaundice seem to result more frequently from intrahepatic biliary obstruction than from pressure or invasion of the portal outlet.[2] The differentiation of cause of jaundice is obviously of importance to the decision about modes of therapy.

Three histologic gradings of Hodgkin's disease proposed by Jackson and Parker[4] are termed *paragranuloma, granuloma* and *sarcoma.* The paragranuloma is characteristically predominantly composed of adult lymphocytes. Careful search is often required to find the Reed-Sternberg cells. When Reed-Sternberg cells are mostly mononuclear without globing, being presumably early forms, the distinction between paragranuloma and lymphocytic lymphosarcoma may be difficult. Paragranuloma, or even granuloma, may also in some cases be read into biopsy slides that other pathologists would interpret as showing chronic lymphadenitis. This distinction is naturally of paramount importance to the clinician; but in some cases, further lapses of time and study of further biopsy material may be the only means of enabling a clear-cut decision.

Hodgkin's granuloma, while usually showing the characteristic cellular complex, nevertheless is sometimes difficult to distinguish from other granulomatous or other changes in lymph node structure. Examples of other processes whose histologic features may, on occasion, be mistaken for those of Hodgkin's granuloma are many. In the Hodgkin's granuloma, the nuclei of the Reed-Sternberg cells are mostly multilobed or, less often, multiple with prominent nuclei. Histologically characteristic of Hodgkin's granuloma is a mixture of granulocytes, fibroblasts, lymphocytes, plasma cells, monocytes and histiocytes, often with areas of necrosis and at times more or less extensive fields of fibrosis. But, in all this variety, the one essential diagnostic criterion is the Reed-Sternberg cell.

Summary

Acute cholecystitis is most often associated with gallbladder calculi obstructing the cystic duct. A case of Hodgkin's disease involving the cystic duct of the gallbladder causing obstruction is presented and discussed. The absence of most of the usual signs of acute cholecystitis in the case reported is noted.

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—ALBERT E. SLOANE, M.D., Boston

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